ORIGINAL ARTICLE

Targeted Use of Computed Tomographic Coronary Angiography in Acute Chest Pain

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ABSTRACT

BACKGROUND

Many patients with suspected acute coronary syndrome in whom myocardial infarction has been ruled out in the emergency department remain at risk for cardiovascular events. Whether further investigation reduces this risk is unknown.

METHODS

In a multicenter, randomized, controlled trial, patients who presented to an emergency department in 14 hospitals across the United Kingdom were enrolled if myocardial infarction had been ruled out and high-sensitivity cardiac troponin testing indicated an intermediate risk of a cardiovascular event (maximum high-sensitivity cardiac troponin I or T concentration, >5 ng per liter). Participants were randomly assigned in a 1:1 ratio to receive either outpatient computed tomographic (CT) coronary angiography–guided care or standard care. The primary outcome was a composite of myocardial infarction or death from a cardiac cause.

RESULTS

From September 18, 2019, to May 11, 2023, a total of 3170 participants (median age, 61 years; female sex, 30.2%) were assigned to undergo CT coronary angiography (1587 participants) or receive standard care (1583 participants). At 90 days after randomization, CT coronary angiography had been performed in 1462 participants (92.1%) in the CT coronary angiography group and in 35 participants (2.2%) in the standard-care group. Overall, 7 participants (0.4%) had a CT coronary angiography–related adverse event. After a median of 3.0 years, at which point the number of primary-outcome events in the standard-care group exceeded the prespecified minimum of 97, a primary-outcome event had occurred in 112 participants (7.1%) in the CT coronary angiography group and in 116 (7.3%) in the standard-care group (adjusted hazard ratio, 0.95; 95% confidence interval, 0.73 to 1.23; P=0.71).

CONCLUSIONS

In patients with suspected acute coronary syndrome in whom myocardial infarction had been ruled out, routine CT coronary angiography–guided management did not result in a lower incidence of subsequent myocardial infarction or death from a cardiac cause than standard care. (Funded by the British Heart Foundation; TARGET-CTCA ClinicalTrials.gov number, NCT03952351.)

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Patients presenting with acute chest pain account for 5 to 10% of all emergency department visits, with assessment of these patients placing a substantial burden on health care systems and resources.[1-3] Accelerated diagnostic pathways that use high-sensitivity cardiac troponin tests to rule out myocardial infarction at presentation have enabled safe discharge from the emergency department and reduced hospital admissions.[4,5] In patients in whom myocardial infarction is ruled out, cardiac troponin testing provides information regarding subsequent risk and could aid in the identification of patients who would benefit from further investigation, preventative therapies, or coronary revascularization.[6,7]

Patients with very low troponin concentrations remain at low risk for myocardial infarction or death from a cardiac cause for up to 5 years.[8] In contrast, those who are at intermediate risk according to high-sensitivity cardiac troponin testing are twice as likely as those with very low troponin concentrations to have coronary artery disease on computed tomographic (CT) coronary angiography[9] and are 10 times as likely to have a subsequent myocardial infarction or die from a cardiac cause within 1 year after testing.[7,10] Consequently, clinical practice guidelines recommend consideration of CT coronary angiography or noninvasive stress imaging in patients with suspected acute coronary syndrome who are at intermediate risk.[11-13] However, the type of additional investigation that should be undertaken is unclear, and there is currently no evidence that any investigation alters clinical outcomes. We designed the present trial to determine whether performing early outpatient CT coronary angiography leads to a reduction in the risk of subsequent myocardial infarction or death from a cardiac cause among patients with suspected acute coronary syndrome but without myocardial infarction who are considered to be at intermediate risk.[14]

Methods

Trial Design and Oversight

The Troponin in Acute Chest Pain to Risk Stratify and Guide Effective Use of Computed Tomography Coronary Angiography (TARGET-CTCA) trial was a multicenter, open-label, event-driven, randomized trial with blinded end-point assessment. The trial design has been published previously.[14] The trial protocol (available with the full text of this article at NEJM.org) was reviewed and approved by the South-East Scotland Research Ethics Committee and was periodically reviewed by an independent data monitoring committee. The trial was performed in accordance with the principles of the Declaration of Helsinki and with written informed consent from all the participants.

Trial Participants

Adult patients (≥18 years of age) who presented to an emergency department or acute medical assessment center with suspected acute coronary syndrome were eligible for enrollment. Patients could be included if myocardial infarction had been ruled out but they were at intermediate risk for future myocardial infarction on the basis of a maximum high-sensitivity cardiac troponin I or T concentration between the low-risk threshold of 5 ng per liter[10,15] and the sex-specific 99th percentile of the upper reference limit (Fig. S1 in the Supplementary Appendix, available at NEJM.org).[16,17] To ensure that the trial was inclusive and representative, potential participants who were not approached in the hospital were identified with the use of electronic medical records and contacted by telephone. Additional exclusion criteria are listed in Table S1.

Intervention and Procedures

After providing consent, participants were randomly assigned in a 1:1 ratio to receive either CT coronary angiography–guided care plus standard care (CT coronary angiography group) or standard care alone (standard-care group). Randomization was performed with a Web-based computer-generated system to ensure concealment of group assignment and was stratified according to site, age (<70 or ≥70 years), sex, and the presence or absence of known coronary artery disease. Trial participants who were assigned to the standard-care group had no further trial visits. Those assigned to the CT coronary angiography group were invited to undergo outpatient CT coronary angiography with a 64-slice or higher multidetector scanner as soon as possible after their initial hospital visit (ideally within 4 weeks after randomization).

Imaging results were reported according to the Society of Cardiovascular Computed Tomography guidelines.[18] Coronary arteries were classified as normal (diameter stenosis of <10%) or as having mild (diameter stenosis of 10 to 49%), moderate

(diameter stenosis of 50 to 70%), or obstructive (diameter stenosis of >70% or of >50% in the left main stem) coronary artery disease. Results, including any clinically significant noncardiac findings, were provided to the participant, primary care physician, and other health care professionals involved in clinical care. The report included a recommendation to commence secondary preventative therapy in participants with mild coronary artery disease (statin therapy alone) or moderate nonobstructive or obstructive coronary artery disease (both antiplatelet and statin therapies) (Fig. S2). In addition, those with obstructive disease or clinically important noncardiac findings were offered an outpatient consultation, ideally within 2 weeks after obtaining the CT coronary angiography scan result.

TRIAL OUTCOMES

Follow-up data were obtained from medical records at 90 days and annually thereafter and from participant questionnaires at 90 days and at 1 and 2 years. All the participants underwent follow-up until the minimum number of primary-outcome events had accrued. The primary outcome was a composite of myocardial infarction or death from a cardiac cause. Myocardial infarction was defined according to the Fourth Universal Definition of Myocardial Infarction.[16] Death from a cardiac cause was defined as death resulting from an acute myocardial infarction or heart failure or death from a sudden cardiac cause.[19] All deaths and all hospital admissions for suspected acute coronary syndrome or myocardial injury were adjudicated by two independent clinicians who were unaware of the trial intervention, with any discrepancies resolved by a third clinician as described previously.[20] Secondary outcomes included clinical, participant-reported, process, and cost-effectiveness outcomes and are listed and defined in Tables S2 and S3, respectively.

STATISTICAL ANALYSIS

Baseline characteristics are summarized for each trial group. On the basis of the event rates in a previous trial[20] and the relative risk reductions observed in a trial of CT coronary angiography in participants with stable chest pain,[21] our trial was designed to have 90% power to detect a 40% difference between the groups in the incidence of a primary-outcome event. We planned to include 2270 participants to account for a loss to follow up of 5%; at least 97 primary-outcome events were required in the standard-care group for the trial to be conclusive, which was anticipated to occur at a median follow-up of 36 months. On April 25, 2022, a blinded assessment of the number of events that had accrued among the first 1925 participants was performed, and the data monitoring committee concluded that the trial would not reach the required number of events by the planned follow-up date in September 2024. This finding was a consequence of interruptions in recruitment owing to the coronavirus disease 2019 pandemic, with most participants having less than 12 months of follow-up at this point. To minimize the likelihood that follow-up would need to be extended, the data monitoring committee recommended that recruitment continue until 3170 participants had been enrolled.

The primary and secondary analyses were based on the intention-to-treat principle and included all outcomes that had occurred from randomization to the trial end date. Follow-up continued until at least 97 primary-outcome events had accrued in the standard-care group. Outcomes were compared with the use of a Cox proportional-hazards model, and the effects of the intervention were expressed as hazard ratios with corresponding 95% confidence intervals and a P value. The model was adjusted for site, age, sex, and previous coronary artery disease. The proportional-hazards assumption was assessed and confirmed to be satisfied. A supplementary analysis was performed with the use of the Fine–Gray model to account for competing risks. In the secondary analysis, the effect of the intervention on the odds of myocardial infarction or death from a cardiac cause occurring within 2 years was evaluated with a logistic-regression model that was adjusted for the same variables as those in the Cox proportional-hazards model. Sensitivity analyses included landmark and per-protocol analyses (see the Supplementary Appendix). Subgroup analyses were performed by examining the effect of the intervention according to subgroup in the adjusted Cox regression model.

Secondary outcomes were analyzed with logistic regression for binary outcomes and linear regression for normally distributed continuous outcomes, with adjustment for the same variables as for the primary outcome. The secondary outcomes were exploratory in nature, with no adjustment for multiple testing; thus, the 95% confi-

dence intervals should not be used in place of hypothesis testing. Survival times were summarized with Kaplan–Meier survival curves. All reported analyses were prespecified in a statistical analysis plan (available with the protocol at NEJM.org) and performed with SAS software, version 9.4 (SAS Institute), and R software, version 4.5.2 (R Project for Statistical Computing).

RESULTS

TRIAL PARTICIPANTS

From September 18, 2019, to May 11, 2023, a total of 3170 participants (median age, 61 years [interquartile range, 53 to 70]; female sex, 30.2%) were enrolled at 14 hospitals (Table S4): 1587 were randomly assigned to the CT coronary angiography group and 1583 to the standard-care group at a median of 6 days (interquartile range, 3 to 9) after presentation (Fig. S3). On December 4, 2025, a total of 97 primary-outcome events had accrued in the standard-care group and sites were asked to complete an end-of-trial review. After database lock, the trial concluded on May 25, 2026; the median follow-up was 3.0 years (interquartile range, 3.0 to 4.0).

Overall, characteristics of the participants were balanced between the two groups (Table 1 and Table S5) and were representative of patients with suspected acute coronary syndrome in the United Kingdom (Table S6). Of 3166 participants with available data, 2809 (88.7%) presented with chest discomfort, 553 (17.5%) had a previous diagnosis of myocardial infarction, and 478 (15.1%) had a previous diagnosis of angina. The mean (±SD) History, Electrocardiogram, Age, Risk Factors, and Troponin (HEART) score was 3.5±1.4, with 1566 of 3152 participants (49.7%) classified as having intermediate or high risk on the basis of a score greater than 3.[22,23] HEART scores range from 0 to 10, with scores of 0 to 3 indicating low risk, 4 to 6 intermediate risk, and 7 to 10 high risk. At randomization, 921 of 3164 participants (29.1%) were taking an antiplatelet agent and 1373 of 3165 participants (43.4%) were taking a statin.

TRIAL INTERVENTION

In the CT coronary angiography group, 1462 participants (92.1%) underwent CT coronary angiography, with imaging performed a median of 22 days (interquartile range, 13 to 36) after randomization. Among these participants, normal coronary arteries were identified in 465 (31.8%), nonobstructive coronary artery disease in 622 (42.5%), and obstructive coronary artery disease in 331 (22.6%) (Table 2). Among the participants who underwent trial CT coronary angiography, 617 (42.2%) had noncardiac findings, and 157 (10.7%) were considered by the investigator to have clinically significant findings (Table S7).

In the standard-care group, nontrial CT coronary angiography was performed in 35 participants (2.2%) within 90 days after randomization and in 103 participants (6.5%) by the end of the trial. Invasive coronary angiography was performed in 177 participants (11.2%) in the CT coronary angiography group and in 137 participants (8.7%) in the standard-care group, with noninvasive stress testing performed in 133 participants (8.4%) and 153 participants (9.7%), respectively.

CARE MANAGEMENT

Among the 1568 participants with available data in the CT coronary angiography group, 665 participants (42.4%) were receiving an antiplatelet agent and 994 (63.4%) were receiving statin therapy 90 days after randomization. Among the 1568 participants with available data in the standard-care group, 515 participants (32.8%) were receiving an antiplatelet agent and 760 (48.5%) were receiving statin therapy 90 days after randomization (Table 2 and Table S8). Percutaneous or surgical coronary revascularization had been performed in 26 participants (1.6%) in the CT coronary angiography group and in 15 participants (0.9%) in the standard-care group at 90 days and in 98 participants (6.2%) and 77 participants (4.9%), respectively, at the end of the trial.

PRIMARY AND SECONDARY OUTCOMES

During the follow-up period, a primary-outcome event occurred in 112 participants (7.1%) in the CT coronary angiography group and in 116 participants (7.3%) in the standard-care group (adjusted hazard ratio for myocardial infarction or death from a cardiac cause, 0.95; 95% confidence interval [CI], 0.73 to 1.23; P=0.71) (Table 3, Fig. 1, and Table S9). No meaningful difference in the incidence of a primary-outcome event was observed between the two groups when assessed with adjustment for competing risks, at 2 years, or in landmark, per-protocol, or post hoc sensi-

Table 1. Characteristics of the Trial Participants at Randomization.*

Characteristic	CT Coronary Angiography (N=1587)	Standard Care (N=1583)
Median age (IQR) — yr	61.0 (52.0–69.0)	61.0 (53.0–70.0)
Female sex — no. (%)	479 (30.2)	477 (30.1)
Cardiovascular risk factors		
Body-mass index†	29.5±6.0	29.5±6.1
Diabetes mellitus — no./total no. (%)	237/1585 (15.0)	216/1581 (13.7)
Hypertension — no./total no. (%)	724/1585 (45.7)	697/1581 (44.1)
Family history of coronary artery disease — no./total no. (%)	626/1576 (39.7)	545/1576 (34.6)
Current cigarette smoker — no./total no. (%)	210/1584 (13.3)	204/1581 (12.9)
Former smoker — no./total no. (%)	606/1584 (38.3)	605/1581 (38.3)
Medical history — no./total no. (%)		
Previous myocardial infarction	283/1585 (17.9)	270/1581 (17.1)
Known angina	236/1585 (14.9)	242/1581 (15.3)
Coronary revascularization — no./total no. (%)		
Previous percutaneous coronary intervention	246/1584 (15.5)	236/1581 (14.9)
Previous coronary-artery bypass grafting	51/1585 (3.2)	42/1581 (2.7)
Medications at randomization — no./total no. (%)		
Antiplatelet therapy‡	452/1584 (28.5)	469/1580 (29.7)
Statin	689/1584 (43.5)	684/1581 (43.3)
Preventative medication§	760/1584 (48.0)	747/1581 (47.2)
ACE inhibitor or ARB	610/1584 (38.5)	557/1581 (35.2)
Beta-blocker	384/1584 (24.2)	372/1581 (23.5)
Chest discomfort at presentation — no./total no. (%)	1397/1585 (88.1)	1412/1581 (89.3)
Electrocardiogram — no./total no. (%)		
Q waves	52/1566 (3.3)	52/1557 (3.3)
ST-segment elevation	44/1564 (2.8)	45/1556 (2.9)
ST-segment depression	18/1563 (1.2)	25/1556 (1.6)
T-wave inversion	243/1566 (15.5)	228/1557 (14.6)
Left or right bundle-branch block	123/1564 (7.9)	121/1557 (7.8)
Risk scores		
Mean GRACE score¶	91±23	91±24
GRACE score ≥109 — no./total no. (%)¶	722/1354 (53.3)	700/1332 (52.6)
Mean HEART score‖	3.5±1.4	3.6±1.4
HEART score >3 — no./total no. (%)‖	796/1576 (50.5)	770/1576 (48.9)
Hematologic findings and clinical chemical variables		
Hemoglobin — g/dl	14.4±1.4	14.4±1.4
Estimated glomerular filtration rate — ml/min	63±10	63±10
Median maximal high-sensitivity cardiac troponin I (IQR) — ng/liter	8.0 (6.0–11.0)	8.0 (6.0–11.0)
Median maximal high-sensitivity cardiac troponin T — ng/liter	8.0 (7.0–10.0)	8.0 (7.0–10.0)

* Plus–minus values are means ±SD. ACE denotes angiotensin-converting enzyme, ARB angiotensin-receptor blocker, CT computed tomographic, and IQR interquartile range.
† Body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ Antiplatelet therapy included aspirin or a P2Y12 antagonist.
§ Preventative medication included any antiplatelet agent or a statin.
¶ Global Registry of Acute Coronary Events (GRACE) scores range from 0 to 383, with scores of 0 to 108 indicating low risk, scores of 109 to 140 intermediate risk, and scores of 141 to 383 high risk.
‖ History, Electrocardiogram, Age, Risk Factors, and Troponin (HEART) scores range from 0 to 10, with scores of 0 to 3 indicating low risk, scores of 4 to 6 intermediate risk, and scores of 7 to 10 high risk.

Table 2. Investigations and Care Management after Randomization.*

Variable	CT Coronary Angiography (N=1587)	Standard Care (N=1583)
CT coronary angiography		
Underwent as randomly assigned — no. (%)	1462 (92.1)	—
Underwent although not randomly assigned — no. (%)		
Within 90 days	—	35 (2.2)
By the end of the trial	—	103 (6.5)
Normal coronary arteries — no./total no. (%)	465/1462 (31.8)	—
Coronary artery disease — no./total no. (%)		
Nonobstructive	622/1462 (42.5)	—
Obstructive	331/1462 (22.6)	—
In proximal left anterior descending artery	132/1462 (9.0)	—
In left main stem	11/1462 (0.8)	—
One-vessel	201/1462 (13.7)	—
Two-vessel	87/1462 (6.0)	—
Three-vessel	43/1462 (2.9)	—
Median CAD-RADS score (IQR)†	2.0 (0.0–3.0)	—
Median segment involvement score (IQR)‡	2.0 (0.0–5.0)	—
Median segment stenosis score (IQR)§	2.0 (0.0–7.0)	—
CT coronary angiography was nondiagnostic or data were missing — no./total no. (%)	44/1462 (3.0)	—
Noncardiac findings — no./total no. (%)	617/1462 (42.2)	—
Clinically significant noncardiac findings — no./total no. (%)	157/1462 (10.7)	—
Other cardiac investigations — no. (%)		
Invasive coronary angiography	177 (11.2)	137 (8.7)
Noninvasive stress imaging	133 (8.4)	153 (9.7)
Outpatient visit — no. (%)		
Cardiology at 90 days	424 (26.7)	264 (16.7)
Other specialty at 90 days	91 (5.7)	84 (5.3)
Cardiology at end of trial	799 (50.3)	598 (37.8)
Medical therapy — no./total no. (%)		
Antiplatelet agent at 90 days¶	665/1568 (42.4)	515/1568 (32.8)
Antiplatelet agent at end of trial¶	619/1492 (41.5)	462/1462 (31.6)
Statin at 90 days	994/1568 (63.4)	760/1568 (48.5)
Statin at end of trial	1024/1492 (68.6)	813/1462 (55.6)
Preventative medication at 90 days‖	1046/1568 (66.7)	820/1568 (52.3)
Preventative medication at end of trial‖	1070/1492 (71.7)	854/1462 (58.4)
Coronary revascularization — no. (%)		
PCI or CABG		
At 90 days	26 (1.6)	15 (0.9)
At end of trial	98 (6.2)	77 (4.9)

* CABG denotes coronary-artery bypass grafting, and PCI percutaneous coronary intervention.
† Coronary Artery Disease Reporting and Data System (CAD-RADS) scores range from 0 to 5, with higher scores indicating more atherosclerotic plaque or severe stenosis.
‡ Segment involvement scores range from 0 to 16, with higher scores indicating more widespread plaque.
§ Segment stenosis scores range from 0 (no stenosis) to 5 (complete occlusion).
¶ Antiplatelet agents included aspirin or a P2Y12 antagonist.
‖ Preventative medication included any antiplatelet agent or a statin.

Table 3. Primary and Secondary Outcomes.

Outcome	CT Coronary Angiography (N=1587)	Standard Care (N=1583)	Adjusted Hazard Ratio or Odds Ratio (95% CI)*
	no. of participants (%)		
Primary outcome			
Myocardial infarction or death from a cardiac cause	112 (7.1)	116 (7.3)	0.95 (0.73–1.23)†
Secondary outcomes			
Myocardial infarction	93 (5.9)	100 (6.3)	0.92 (0.69–1.22)
Death from a cardiac cause	23 (1.4)	27 (1.7)	0.83 (0.48–1.45)
Death from any cause	73 (4.6)	97 (6.1)	0.74 (0.54–1.00)
Death from noncardiovascular cause	41 (2.6)	64 (4.0)	0.63 (0.43–0.93)
Death from cardiovascular cause	32 (2.0)	33 (2.1)	0.95 (0.58–1.54)
Myocardial infarction or death from cardiovascular cause	121 (7.6)	121 (7.6)	0.99 (0.77–1.27)
Return visit for suspected acute coronary syndrome	640 (40.3)	602 (38.0)	1.11 (0.96–1.28)
Unscheduled coronary revascularization	38 (2.4)	42 (2.7)	0.90 (0.58–1.41)
Major bleeding‡	6 (0.4)	3 (0.2)	2.02 (0.50–8.08)

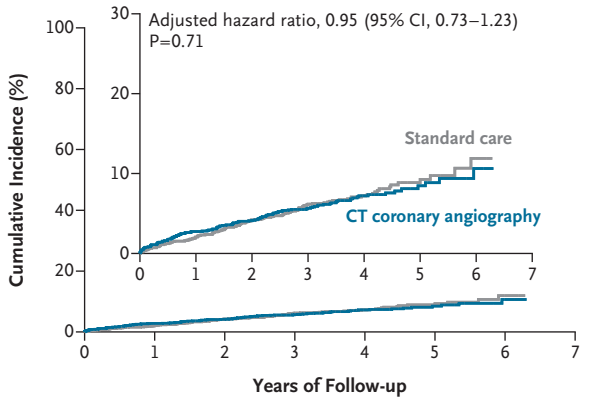
* Values are odds ratios for hospital readmission for suspected acute coronary syndrome, unscheduled coronary revascularization, and major bleeding; all other values are adjusted hazard ratios. Both hazard ratios and odds ratios were adjusted for site, age, sex, and previous coronary artery disease. The 95% confidence intervals for secondary outcomes were not adjusted for multiplicity and should not be used in place of hypothesis testing.
† P=0.71.
‡ Major bleeding was defined as Bleeding Academic Research Consortium (BARC) type 3 to 5 bleeding. BARC types range from 0 to 5, with higher values indicating greater severity of bleeding.

tivity analyses (Table S10). In the CT coronary angiography group, a primary-outcome event occurred in 10 of the 465 participants (2.2%) without coronary artery disease, in 40 of the 622 participants (6.4%) with nonobstructive coronary artery disease, and in 38 of the 331 participants (11.5%) with obstructive coronary artery disease. None of the participants were missing data for the primary outcome, and the time-to-event analysis was therefore performed with complete outcome data for all the participants.

The effect of the trial intervention on the primary outcome appeared to be generally consistent in analyses of prespecified subgroups (Fig. 2) as well as in post hoc analyses (Fig. S4). Analysis of the subgroup stratified according to HEART score appeared to favor CT coronary angiography–guided care in low-risk participants.

There were no apparent differences between the two trial groups with respect to most secondary outcomes, including myocardial infarction, death from a cardiac cause, or death from a cardiovascular cause (Table 3). Death from any cause occurred in 73 participants (4.6%) in the CT coronary angiography group and in 97 participants (6.1%) in the standard-care group (adjusted hazard ratio, 0.74; 95% CI, 0.54 to 1.00) (Table 3 and Fig. S5); deaths from noncardiovascular causes accounted for 41 and 64 of these deaths, respectively (adjusted hazard ratio, 0.63; 95% CI, 0.43 to 0.93). However, secondary and subgroup analyses were not adjusted for multiplicity, which precludes causal conclusions.

Process outcomes and participant-reported outcomes did not appear to differ materially between the groups (Tables S11 and S12). CT coronary angiography–related adverse events were infrequent, with 7 participants (0.4%) having an allergic reaction to or acute kidney injury from contrast medium. Three events (presumed allergic reactions) were categorized as serious by site investigators, but symptoms in all cases were mild and resolved



No. at Risk								
Standard care	1583	1523	1467	1203	619	222	53	0
CT coronary angiography	1587	1525	1487	1232	639	242	61	0
Cumulative No. of Events								
Standard care	0	32	65	94	104	113	116	116
CT coronary angiography	1	43	65	88	104	109	112	112

Figure 1. Incidence of Myocardial Infarction or Death from a Cardiac Cause.
Shown are Kaplan–Meier survival curves for the incidence of myocardial infarction or death from a cardiac cause (the composite primary outcome) among patients assigned to receive either computed tomographic (CT) coronary angiography–guided care or standard care. The inset shows the same data on an expanded y axis.

with no intervention (2 cases) or after treatment with an antihistamine (1 case) (Table S11).

DISCUSSION

In this large, prospective, multicenter, randomized trial involving participants with suspected acute coronary syndrome in whom myocardial infarction had been ruled out and troponin levels suggested intermediate risk, use of early outpatient CT coronary angiography to guide care did not reduce the incidence of subsequent myocardial infarction or death from a cardiac cause. The approach to further cardiac investigation in patients with suspected acute coronary syndrome after the ruling out of myocardial infarction varies markedly worldwide.[24] Clinical practice guidelines in the United States recommend performing CT coronary angiography in patients with acute chest pain who are considered to be at intermediate risk (defined as a risk of a cardiovascular event of ≥1% at 30 days) in order to rule out obstructive coronary artery disease (level 1A recommendation).[13] In Europe, clinical practice guidelines recommend consideration of CT coronary angiography or noninvasive stress imaging in patients with suspected acute coronary syndrome without elevated cardiac troponin levels (level IIa, class A recommendation).[12] These recommendations are based on randomized trials that evaluated the effect of CT coronary angiography on length of stay in or discharge from the emergency department[25-28] and that were performed before the widespread adoption of high-sensitivity cardiac troponin testing for risk stratification within accelerated diagnostic pathways to support the safe discharge of low-risk patients.[4,7,11]

In our trial, CT coronary angiography–guided care did not lead to a lower incidence of myocardial infarction or death from a cardiac cause at 3 years than standard care despite enrollment of patients known to be at intermediate risk for cardiovascular events owing to cardiac troponin concentrations.[6,10,29,30] The population was representative of patients with suspected acute coronary syndrome in the United Kingdom, with participants across 14 hospitals being enrolled and 75.6% of those eligible for inclusion after screening undergoing randomization. The intervention was performed successfully in 92.1% of the participants, with only 2.2% undergoing nontrial CT coronary angiography in the standard-care group at 90 days. In the CT coronary angiography group, two thirds of the participants had coronary artery disease and were receiving preventative therapy at 90 days. Our findings appeared to be consistent across all high-risk subgroups and in the subgroup of participants without a previous diagnosis of coronary artery disease who may have been most likely to benefit from the intervention.

The Coronary Computed Tomographic Angiography in Intermediate-Risk Chest Pain Patients (FAST-CCTA) trial (ClinicalTrials.gov number, NCT04748237) is ongoing and will evaluate whether performing CT coronary angiography in patients presenting to the emergency department with chest pain who have a HEART score greater than 3 reduces the risk of death, myocardial infarction, or unstable angina. In our trial, analyses of subgroups that were stratified according to HEART score did not show a greater benefit of CT coronary angiography among participants with a score greater than 3 than among those with a score of 3 or lower.

Subgroup	Total No. of Participants (%)	CT Coronary Angiography	Standard Care	Adjusted Hazard Ratio (95% CI)
		no. of participants with event/total no. (%)		
Overall	3170 (100.0)	112/1587 (7.1)	116/1583 (7.3)	0.95 (0.73–1.23)
Sex				
Male	2214 (69.8)	78/1108 (7.0)	92/1106 (8.3)	0.83 (0.61–1.12)
Female	956 (30.2)	34/479 (7.1)	24/477 (5.0)	1.44 (0.85–2.43)
Age				
<70 yr	2372 (74.8)	63/1191 (5.3)	61/1181 (5.2)	1.02 (0.72–1.46)
≥70 yr	798 (25.2)	49/396 (12.4)	55/402 (13.7)	0.87 (0.59–1.28)
Known coronary artery disease				
Yes	779 (24.6)	57/390 (14.6)	58/389 (14.9)	0.95 (0.66–1.38)
No	2391 (75.4)	55/1197 (4.6)	58/1194(4.9)	0.95 (0.66–1.37)
Receiving preventative therapy				
Yes	1507 (47.6)	74/760 (9.7)	85/747 (11.4)	0.84 (0.61–1.14)
No	1658 (52.4)	38/824 (4.6)	31/834 (3.7)	1.27 (0.79–2.05)
High-sensitivity assay				
Cardiac troponin I	1703 (53.7)	80/851 (9.4)	87/852 (10.2)	0.90 (0.66–1.22)
Cardiac troponin T	1467 (46.3)	32/736 (4.3)	29/731 (4.0)	1.10 (0.66–1.81)
Cardiac troponin concentration				
<Median	1331 (42.0)	30/660 (4.5)	34/671 (5.1)	0.93 (0.57–1.52)
≥Median	1835 (58.0)	82/925 (8.9)	82/910 (9.0)	0.94 (0.69–1.28)
HEART score				
Low risk	1586 (50.3)	22/780 (2.8)	39/806 (4.8)	0.58 (0.35–0.98)
Intermediate or high risk	1566 (49.7)	88/796 (11.1)	76/770 (9.9)	1.11 (0.81–1.50)

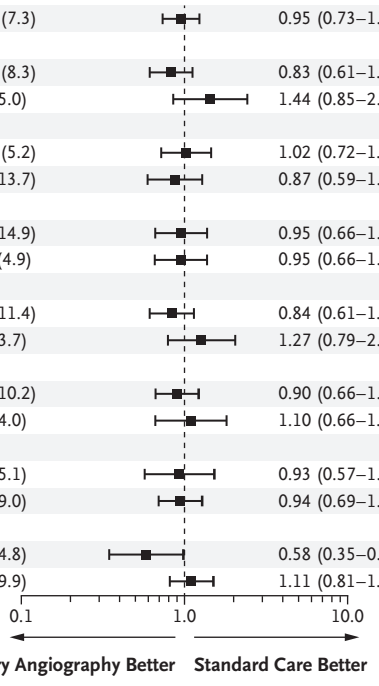


Figure 2. Incidence of Myocardial Infarction or Death from a Cardiac Cause in Prespecified Subgroups.

Shown is a forest plot of the incidence of myocardial infarction or death from a cardiac cause (the composite primary outcome) among patients assigned to receive either CT coronary angiography–guided care or standard care, with stratification according to prespecified subgroups. Preventative therapy included any antiplatelet agent or statin received at randomization. Cardiac troponin concentration reflects sex- and assay-specific median maximum cardiac troponin concentrations. The History, Electrocardiogram, Age, Risk Factors, and Troponin (HEART) score ranges from 0 to 10, with scores of 3 or lower indicating low risk and scores higher than 3 indicating intermediate or high risk.

The incidence of death from any cause and death from noncardiovascular causes appeared to be lower in the CT coronary angiography group than in the standard-care group. We did not control for multiple hypothesis testing, and causal conclusions cannot be made. We did not collect data to inform whether the detection of noncardiac findings, which occurred in 42.2% of the participants, altered care.

Our trial has some limitations. First, the incidence of a primary-outcome event at 1 year was lower than projected on the basis of our previous trial.[4] To ensure that the trial was suitably powered, we used an event-driven design and identified more events during follow-up than planned. Still, the confidence intervals around the hazard ratio are compatible with as much as a 27% reduction to a 23% increase in the incidence of a primary-outcome event. Second, the trial enrolled participants classified as being at intermediate risk according to troponin concentrations, but only half the participants were classified as being at intermediate risk according to risk scores. Third, most of the participants in our trial were men. Acute coronary syndrome is less common in women, and the female sex–specific 99th percentile for troponin concentration is lower,[17] which results in the classification of fewer female patients as being at intermediate risk. Fourth, a proportion of the trial participants were known to have coronary artery disease or were receiving preventative therapy and may have had less benefit from the intervention, which could explain the modest differences in the use of preventative medications between groups. Fifth, our trial was conducted in the United Kingdom, where the pro-

portion of patients undergoing functional or anatomical imaging for coronary artery disease is low.[31] However, this fact would be expected to increase the probability that CT coronary angiography would affect management and improve outcomes; it seems unlikely that CT coronary angiography would be more likely to reduce the incidence of cardiac events in health care systems in which higher proportions of patients undergo imaging investigation as the standard of care.

In this multicenter trial, the use of CT coronary angiography to guide treatment in patients with suspected acute coronary syndrome in whom myocardial infarction was ruled out did not reduce the incidence of subsequent myocardial infarction or death from a cardiac cause.

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